

Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

STUDIES ON AN INHERITED CATARACT
OF SHEEP

A thesis presented in partial fulfilment (30%) of the
requirements for the degree of Master of
Veterinary Science at
Massey University

HOWARD VERNON BROOKS

1981

ABSTRACT

The findings presented in this thesis comprise the first report and description of an inherited cataract in sheep. The condition was first diagnosed in a number of related New Zealand Romney sheep, from a high performance Romney stud.

Clinically, cataracts which are always bilateral, are usually first visible at 2 months of age as characteristic focal opacities, confined to either the central or peripheral anterior and posterior cortex of the lens. By 8 to 10 months of age, there is more generalised lenticular opacity and total opacity usually occurs by 10 to 12 months. Two lambs born with congenital bilateral mature cataracts, showed partial lens absorption, which was obvious clinically by 8 months of age.

Controlled breeding studies, show that cataracts are inherited as a simple autosomal dominant trait. The two congenitally affected lambs, which resulted from matings between affected parents, are assumed to be homozygous for the defective gene.

Histologically, ovine cataract is characterised by the progressive degenerative swelling and lysis of lenticular fibres, beginning initially within localised areas of the anterior and posterior cortex. The distribution of early lesions correlates with the clinical appearance of early stage cataracts. With cataract progression, more of the cortical and eventually the nuclear fibres are affected and in the mature state, only a small number of attenuated equatorial fibres remain. The anterior epithelial cells become vacuolated apparently in response to cortical degeneration, and they also undergo proliferation, metaplasia to a spindle shaped cell and they migrate posteriorly beneath the posterior capsule. Beneath the posterior capsule, epithelial cells form either a single layer of flattened cells, or aggregations of large 'bladder' cells. The formation of new lens fibres at the equator continues relatively normally, throughout all stages of cataract.

Ultrastructurally, anterior epithelial cells contain two types of vacuole. Small circular vacuoles which are not membrane bound are present in small groups within the cytoplasm. These are also present and are more numerous within spindle shaped cells. The large irregular shaped vacuoles noted by light microscopy are usually membrane bound and often contain membranous or granular material. These vacuoles are interpreted as being dilated and damaged endoplasmic reticulum. Both spindle shaped and vacuolated anterior epithelial cells have increased amounts of endoplasmic reticulum and in spindle shaped cells, fibrillar material and electrondense deposits are present. Capsular material, though observed surrounding some spindle shaped cells histologically, could not be demonstrated ultrastructurally. The profound breakdown of the cellular architecture of the lens is readily demonstrated by scanning electronmicroscopy.

Water and electrolyte analyses of cataractous lenses, show that water and sodium content increases and potassium is lost, during cataractogenesis.

The objectives of this study, were to define the inherited cataract of New Zealand Romney sheep in clinical, genetic and pathological terms, to examine water and electrolyte shifts in cataractous lenses, and to compare the condition with other inherited cataracts of man and other animals. It is concluded, that this ovine cataract though apparently clinically unique, does in pathological and biochemical terms resemble many cataracts of man and animals of different causes. These changes are not aetiologically significant, but merely reflect the limited range of stereotyped reactions which are possible in the cataractous lens. For this reason, it is proposed that this ovine cataract would provide a useful model for fundamental studies on the pathogenesis of cataract.

ACKNOWLEDGMENTS

This thesis represents part of the requirements for a Master of Veterinary Science degree in pathology, which was undertaken in the Department of Veterinary Pathology and Public Health at Massey University.

The majority of the work was undertaken whilst on study leave from the Animal Health Division of the New Zealand Ministry of Agriculture and Fisheries and I am most grateful to the Ministry for the granting of this leave. I must especially thank Dr Bruce Simpson, Superintendent, Palmerston North Animal Health Laboratory, for his support of my application for study leave and his support and consideration throughout the duration of this project. I wish to thank also the veterinary staff of the Palmerston North Animal Health Laboratory, for the concessions made to me throughout the period of study leave and during the completion of this thesis on a part-time basis.

I would like to thank Dr R.D. Jolly for his enthusiasm and assistance as supervisor for this project and for his encouragement and advice during thesis preparation. Dr D.M. West of the Department of Veterinary Clinical Sciences and Dr Jolly were responsible for maintaining the experimental flock prior to this study and organised the 1979 mating programme. Many other people gave advice and offered technical expertise during the course of this project.

I am grateful to Dr C.A. Paterson of the University of Colorado Health Sciences Centre, Denver, Colorado, for helpful advice, for providing a considerable amount of valuable literature and for performing the water and electrolyte analyses on sheep lenses. Mr T. Law devoted a great deal of time and effort to eye photography and also printed all the photographs and light micrographs used in this thesis. Mr D.H. Hopcroft of the Department of Scientific and Industrial Research, gave helpful advice on electronmicroscopy and cut the sections photographed in this thesis. Mr Hopcroft also prepared the specimens for scanning electronmicroscopy. Mr R.J. Bennett printed the electronmicrographs.

Histological sections were prepared by Mrs P.M. Slack and Miss S.L. Malloch, Mrs Slack also assisted with the processing of tissues for electronmicroscopy. I thank them for their cheerful and willing co-operation. Mrs A. Larsen of the Central Photographic Unit drew several diagrams for this thesis.

I am indebted to Mrs E. Bristol for typing services and helpful assistance, to Miss D. Wickes and Miss P. Harvey for typing parts of the draft manuscript and to Mrs F.S. Wicherts for typing the final copy.

I would also like to thank the Massey University farm staff Mr S. Scott, Mr W. Morris and Mr P. Whithead, for their care of and interest in the experimental animals, also Mr A.T. de Cleene for his cheerful assistance in the post-mortem room.

Finally and not least, I wish to thank my wife Penny and my children Nicholas and Amy, for their sacrifices during the duration of my post graduate study.

TABLE OF CONTENTS

	Page
LIST OF TABLES	vii
LIST OF FIGURES	viii
INTRODUCTION	1
CHAPTER I The development and structure of the lens.	2
CHAPTER II Literature review : inherited cataracts.	9
CHAPTER III Ovine cataract : clinical findings.	21
CHAPTER IV Genetics.	25
CHAPTER V Pathology.	29
CHAPTER VI Water and electrolyte changes in cataractous lenses.	39
CHAPTER VII Summary and conclusions.	43
REFERENCES	45

LIST OF TABLES

Table		Page
2.I	Some causes of cataract.	9
4.I	Occurrence of cataracts in the progeny of a cataractous ram mated to normal unrelated ewes.	27
4.II	Occurrence of cataracts in the progeny of a cataractous ram mated to cataractous daughter ewes.	27
6.I	Percentage water and cation concentrations in cataractous lenses at different stages of development, from six sheep.	40

LIST OF FIGURES

Figure		following page
1.1	A diagrammatic representation of the development of the lens. Redrawn from Paterson (1979).	3
1.2	A diagrammatic section through the eye, showing the lens in relation to other structures. Reproduced from Paterson (1979).	3
1.3	A three dimensional diagram of the lens. Reproduced from Kessel and Kardon (1979).	4
1.4	A diagrammatic section through the lens showing the anatomical regions of the lens. Reproduced from Paterson (1979).	4
1.5	A composite drawing of the lens cortex, epithelium, capsule and zonular attachments. Photographed from Kessel and Kardon (1979).	6
1.6	The intermediate zone of the anterior epithelium of the lens, from an 8 month old normal lamb.	6
1.7	The equatorial region of the lens of an 8 month old normal lamb.	6
1.8	The equatorial cortex of the lens from an 8 month old normal lamb. Their nuclei form the lens bow as cortical fibres are displaced toward the centre of the lens.	8
1.9	The anterior cortex of the lens from an 8 month old normal lamb. Cortical fibres are hexagonal in cross section and are precisely arranged in parallel rows.	8

Figure		following page
1.10	Anterior cortical fibres from the lens of an 8 month old normal lamb. The long ribbon like fibres are held together by 'ball and socket' like interlocking processes.	8
1.11	Deep cortical or nuclear fibres from the lens of an 8 month old normal lamb. In this region, surface ridges replace interlocking processes as the means of adhesion between fibres.	8
3.1	Early cataract, showing the irregular clover leaf pattern of central opacity, in the anterior cortex. Lamb 15/80 - 2 months old.	23
3.2	Early cataracts, showing numerous spherical opacities within the anterior cortex. Lamb 38/80 - 2 months old.	23
3.3	Early cataracts in which the spherical opacities are becoming confluent and more prominent. Lamb 38/80 - 5 months old.	23
3.4	Early cataracts showing spoke shaped opacities in the anterior cortex. Lamb 12/80 - 2 months old.	23
3.5	Early cataracts in which peripheral opacities have coalesced, to form radiating spoke like patterns. Lamb 12/80 - 5 months old.	23
3.6	Early cataract showing the spoke like pattern of opacity. Lamb 21/79 - 5 months old.	23
3.7	Mid stage cataract in which opacity has spread to involve more of the anterior cortex. Lamb 10/79 - 8.5 months old.	23

Figure		following page
3.8	Mid stage cataract. Lamb 8/79 - 10 months old	23
3.9	Late stage cataract in which most of the anterior cortex is affected. Lamb 8/79 - 11 months old.	23
3.10	Late stage cataract. Lamb 4/79 - 8 months old.	23
3.11	Late stage cataract in which the central lens is densely opaque, while the equatorial cortex is clearer. This cataract is close to maturity. Lamb 3/79 - 11 months old.	23
3.12	Mature cataract showing total lens opacity in an 11 month old lamb - 4/79.	23
3.13	Congenital mature cataract. Lamb 18/79 - 8 days old.	23
3.14	The same animal as above (figure 3.13), showing partial absorption of the lens at 8 months of age.	23
5.1	A schematic diagram of an ovine lens affected with the central form of early stage cataracts.	31
5.2	Amorphous areas within the anterior cortex of the lens of a 2 month old lamb affected with the central form of early stage cataracts.	31
5.3	Swollen anterior cortical fibres adjacent to an amorphous area in the lens of a 2 month old lamb affected with the central form of early stage cataracts.	31

Figure		following page
5.4	Swollen superficial anterior cortical fibres in the lens of a 2 month old lamb affected with the central form of early stage cataracts. A cystic space containing a small amount of eosinophilic debris is present between the swollen fibres and an amorphous area of lenticular degeneration.	31
5.5	Swollen posterior cortical fibres in the lens of a 2 month old lamb affected with the central form of early stage cataracts.	31
5.6	Vacuolated anterior epithelial cells overlying an area of cortical degeneration in the lens of a 2 month old lamb affected with the central form of early stage cataracts.	31
5.7	A schematic diagram of an ovine lens affected with early stage cataracts of peripheral distribution.	33
5.8	Sub epithelial clefts, intercellular cystic spaces and swollen fibres, within the anterior cortex of the lens of a 3 month*old lamb affected with a peripheral (spoke) form of early stage cataract.	33
5.9	Swollen and pale staining anterior extremities of some of the recently formed cortical fibres in the lens of a 3 month old lamb affected with the peripheral (spoke) form of early stage cataracts.	33
5.10	A schematic diagram of the ovine lens affected with mid stage cataracts.	33

Figure		following page
5.11	Degenerate amorphous areas within the anterior cortex of the lens of an 8.5 month old lamb affected with mid stage cataracts. The overlying anterior epithelial cells are extensively vacuolated.	33
5.12	Epithelial cells migrating from the equator beneath the posterior capsule in the lens of an 8.5 month old lamb affected with mid stage cataracts.	33
5.13	Vacuolated anterior epithelial cells which appear to be the source of the round foamy cells lying free in the degenerate cortex, in the lens of an 8.5 month old lamb affected with mid stage cataracts.	33
5.14	A schematic diagram of an ovine lens affected with late stage cataracts.	33
5.15	Rounded up and swollen fibres within the degenerate amorphous anterior cortex, in the lens of an 8.5 month old lamb affected with late stage cataracts.	33
5.16	Swollen cells and intercellular cystic spaces beneath the posterior capsule, in the lens of an 8.5 month old lamb affected with late stage cataracts.	33
5.17	Disorganisation of the nuclear bow and swelling of the posterior extremities of young cortical fibres, in the lens of an 8.5 month old lamb affected with late stage cataracts.	33

Figure		following page
5.18	Metaplasia of the anterior epithelium from cuboidal to spindle shaped cells, in the lens of an 8.5 month old lamb affected with late stage cataracts.	33
5.19	Migration of epithelial cells beneath the posterior capsule in the lens of a 15 month old sheep with mature cataracts. Beneath the capsule these cells enlarge in an attempt to form lens fibres. These enlarged cells are referred to as 'bladder' cells.	33
5.20	Enlarged epithelial cells (bladder cells) and cystic spaces beneath the posterior capsule, in the lens of a 15 month old sheep with mature cataracts.	33
5.21	Anterior epithelial cell hyperplasia in the lens of a 15 month old sheep affected with mature cataracts.	33
5.22	Duplication of the anterior epithelium and the formation of capsular material beneath the wrinkled capsule, in the lens of a 15 month old sheep affected with mature cataracts.	33
5.23	Large irregular vacuoles and small circular vacuoles within anterior epithelial cells in the lens of a 10 month old lamb with mature cataracts. Small vacuoles are also present within the spindle shaped cells.	34
5.24	Large irregular vacuoles which are partly membrane bound within an anterior epithelial cell, in the lens of a 10 month old lamb with mature cataracts.	34

Figure		following page
5.25	Membranous material within the large vacuoles of an anterior epithelial cell in the lens of a 10 month old lamb with mature cataracts. Mildly dilated membrane systems, interpreted as smooth endoplasmic reticulum, are often associated with these large vacuoles.	34
5.26	Electron dense granular and amorphous material within a large vacuole of an anterior epithelial cell, in the lens of a 10 month old lamb with mature cataracts. Numerous small circular vacuoles are also present.	34
5.27	Electron dense deposits and small circular vacuoles, within a spindle shaped cell in the lens of a 10 month old lamb with mature cataracts.	34
5.28	Electron dense deposits surrounded by a limiting membrane within a spindle shaped cell, in the lens of a 10 month old sheep with mature cataracts. The shape of the enclosed deposits suggests that they may be accumulating within a membrane system, such as the endoplasmic reticulum or golgi apparatus.	34
5.29	Unlined circular vacuoles, abundant rough endoplasmic reticulum and fibrillar material, within the cytoplasm of a spindle shaped cell, in the lens of a 10 month old lamb with mature cataracts.	34
5.30	The anterior epithelium of the lens of a 5 month old normal lamb.	34
5.31	An anterior epithelial cell in the lens of a 5 month old normal lamb.	34

Figure		following page
5.32	Anterior cortical fibres in the lens of a 2 month old normal lamb.	34
5.33	Anterior cortical fibres in the lens of a 2 month old normal lamb.	34
5.34	Anterior cortical fibres in the lens of a 3 month old lamb with early stage cataracts.	34
5.35	Stunted, atrophic, interlocking processes of anterior cortical fibres, in the lens of a 3 month old lamb affected with early stage cataracts.	34
5.36	Mishapen, convoluted, anterior cortical fibres, in the lens of a 4 month old lamb affected with late stage cataracts.	34
5.37	Anterior cortical fibres with a nodular surface and atrophic interlocking processes, in the lens of a 4 month old lamb affected with late stage cataracts .	34
5.38	Degenerate globular shaped fibres, within rows of degenerate cortical fibres in the lens of a 4 month old lamb affected with late stage cataracts.	34
5.39	Degenerate globular fibres within the anterior cortex, in the lens of a 4 month old lamb affected with late stage cataracts.	34

INTRODUCTION

Inherited cataracts have been recorded in man and several animal species. The objectives of this study, were to define a previously unreported ovine inherited cataract in clinical, genetic and pathological terms and to compare these findings with those reported in man and other animals.